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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/738,599	12/15/2000	Lisa K. Nolan	255.0001 0122	1240

26813 7590 01/27/2004

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EXAMINER	
DEVI, SARVAMANGALA J N	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 01/27/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/738,599	Applicant(s) NOLAN ET AL.	
	Examiner S. Devi, Ph.D.	Art Unit 1645	

-- *The MAILING DATE of this communication appears on the cover she t with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *30-33 and 35-70* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *30,31,33 and 69* is/are allowed.

6)☒ Claim(s) *32,37-43,45,67,68 and 70* is/are rejected.

7)☒ Claim(s) *44* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Sequence search report (1).*

DETAILED ACTION

Request for Continued Examination

1) A request for continued examination under 37 C.F.R 1.114, including the fee set forth in 37 C.F.R 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 C.F.R 1.114, and the fee set forth in 37 C.F.R 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 C.F.R 1.114. Applicants' submission filed on 10/15/03 (paper no. 19) has been entered.

Applicants' Amendments

2) Acknowledgment is made of Applicants' amendment filed 09/17/02 and 10/15/02 (paper no. 20 and 16) in response to the final Office Action mailed 04/18/03 (paper no. 14).

Status of Claims

3) Claims 35, 37, 38, 41, 42, 46, 48, 57-59, 61, 63 and 67 have been amended via the amendment filed 09/17/03.

New claims 68-70 have been added via the amendment filed 09/17/03.

Claim 70 has been amended via the amendment filed 10/15/02.

Claims 30-33 and 35-70 are pending.

Claims 30-33, 37-45 and 67-70 are under examination.

Terminal Disclaimer

4) Acknowledgment is made of Applicants' terminal disclaimer filed 09/17/03 (paper no. 17) disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of US patent 6,087,128.

Prior Citation of Title 35 Sections

5) The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior Office Action.

Prior Citation of References

6) The references cited or used as prior art in support of one or more rejections in the instant Office Action and not included on an attached form PTO-892 or form PTO-1449 have been previously cited and made of record.

Rejection(s) Withdrawn

7) The rejection of claims 30-33 made in paragraph 7 of the Office Action mailed 09/30/02 (paper no. 11) and maintained in paragraph 21 of the Office Action mailed 04/18/03 (paper no. 14) under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 17 of U.S. Patent 6,087,128, is withdrawn in light of Applicants' terminal disclaimer disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of US patent 6,087,128.

8) The rejection of claims 37-44 and 67 made in paragraph 7 of the Office Action mailed 09/30/02 (paper no. 11) and made or maintained in paragraph 22 of the Office Action mailed 04/18/03 (paper no. 14) under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5 of the U.S. patent 6,087,128, is withdrawn in light of Applicants' terminal disclaimer disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of US patent 6,087,128.

9) The rejection of claim 42 made in paragraph 9(g) of the Office Action mailed 09/30/02 (paper no. 11) and maintained in paragraph 20 of the Office Action mailed 04/18/03 (paper no. 14) under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

10) The rejection of claim 67 made in paragraph 23 of the Office Action mailed 04/18/03 (paper no. 14) under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

11) The rejection of claims 37-40, 43 and 67 made in paragraph 24 of the Office Action mailed 04/18/03 (paper no. 14) under 35 U.S.C § 102(b) as being anticipated by Barondess *et al.* (*Nature* 344: 871-874, 1990 - Applicants' IDS) (Barondess, 1990), or Chuba *et al.* (*Mol. Gen. Genet.* 216: 287-292, 1989 - Applicants' IDS) as evidenced by Harlow *et al.* (*In*: *Antibodies*: *A laboratory Manual*. Cold Spring Harbor Laboratory, Chapter 5, p. 76, 1988), is withdrawn. Applicant's arguments with respect to this art rejection have been considered but are moot in view of the withdrawal of, or the new ground(s) of rejection.

Rejection(s) under 35 U.S.C § 112, Second Paragraph

12) Claims 32, 45 and 67 are rejected under 35 U.S.C § 112, second paragraph, as being

indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

(a) Claim 32 is incorrect and/or confusing in the recitation 'nucleotides ..... is operably linked'. It is unclear whether nucleotides 73 to 309 are operably linked, or whether the nucleic acid molecule is operably linked to a promoter.

(b) Claim 45 is incorrect and/or confusing in the recitation 'molecule further comprising nucleotides' as opposed to --molecule further comprises nucleotides--.

(c) Claim 67 lacks antecedence for the limitations: 'subunit', and 'fragment'. For proper antecedence, it is suggested that Applicants replace the limitations with --the subunit-- and --the fragment--.

Rejection(s) under 35 U.S.C § 102

13) Claims 37-40, 43 and 67 are rejected under 35 U.S.C § 102(b) as being anticipated by Sanger *et al.* (*J. Mol. Biol.* 162: 729-773, 1982, Applicants' IDS).

Sanger *et al.* taught a nucleic acid molecule comprising several long stretches of nucleotides showing 100% sequence identity with nucleotides 73 to 309 of SEQ ID NO: 22, a plasmid, a phage (viral) vector, and host cells comprising the same. See the attached sequence search report and the entire reference. The nucleic acid molecule contains the ATG start and the SD ribosome binding site and is contained in a buffer or water (i.e., pharmaceutically acceptable carrier). See pages 730-735 and 769; Materials and Methods; and Results and Discussion. A sequence search performed in the Office shows that one of the polypeptides, a fragment or subunit thereof is about 33 amino acid residues-long: KTVDAAKICGGAENVVKTETQQTFVNGLLGFIT which has 100% sequence identity with a fragment of the instant SEQ ID NO. 2. See the gamma strand in Figure 6. The fact that the protein or polypeptide was expressed (see page 762) indicates that the prior art nucleotide sequence inherently contained a regulatory or control sequence. That the 33 amino acid residues-long polypeptide encoded by the prior art nucleotide sequence is long enough to be immunogenic is inherent from the teachings of Sanger *et al.*, absent evidence to the contrary. The functional limitation, "immunogenic" or 'generates an antibody response', on which the prior art reference is silent, is considered to be an inherent property of the prior art product. Where the only difference between claimed product and the prior art product is recited in the functional language, i.e., by what

it does rather than what it is, it is incumbent upon Applicants, when challenged by the USPTO, to demonstrate that the prior art product does not actually possess those characteristics.

Claims 37-40, 43 and 67 are anticipated by Sanger *et al.*

Rejection(s) under 35 U.S.C § 103

14) Claims 37 and 41 are rejected under 35 U.S.C § 103(a) as being unpatentable over Sanger *et al.* (*J. Mol. Biol.* 162: 729-773, 1982 - Applicants' IDS) in view of in view of Applicants' admitted state of the prior art. ?

Claim 37 is included in this rejection since claim 41 includes the limitation 'claim 37'.

The teachings of Sanger *et al.* are explained above which do not expressly disclose that the regulatory or control sequence causes expression of the polypeptide in an animal cell.

However, expression of an art-known nucleic acid molecule via an art-known regulatory or control sequence that causes expression in an animal cell line was routine and conventional in the art at the time of the invention. For instance, Applicants acknowledge in the instant specification the following to be known in the art: transformation and transfection methods; a wide variety of control or promoter sequences, compatible vectors, and eukaryotic expression systems or cell lines known to those skilled in the art of molecular biology to express polynucleotides; the use of vaccinia recombinant plasmid; the production of fusion protein for easy purification; and the standard affinity chromatography and purification methods. See pages 28-34 of the specification.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to express Sanger's nucleic acid molecule or polynucleotide via any one of the admittedly art-known animal or mammalian cell using any one of the admittedly art-known compatible control or regulatory sequences suing art known techniques to produce the instant invention, with a reasonable expectation of success. Expression of Sanger' DNA via an animal cell is well within the realm of routine experimentation. One of skill in the art would have been motivated to produce the instant invention for the expected benefit of improved expression of Sanger's polynucleotide since improved expression is ideally desired in the art.

Claims 37 and 41 are *prima facie* obvious over the prior art of record.

15) Claim 42 is rejected under 35 U.S.C § 103(a) as being unpatentable over Sanger *et al.* (*J. Mol. Biol.* 162: 729-773, 1982 - Applicants' IDS) and Krieg *et al.* (WO 96/02555).

The teachings of Sanger *et al.* are explained above, which do not disclose the their polynucleotide further comprising an immunostimulatory sequence.

However, the use of immunostimulatory sequences, for example, an immunostimulatory oligonucleotide sequence along with a heterologous polynucleotide sequence for the purpose of immunostimulation was well known in the art at the time of the invention. For instance, Krieg *et al.* showed that it was routine and conventional in the art to use a CpG immunostimulatory nucleotide sequence in a pharmaceutical composition (see abstract; and claims).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to express Sanger's nucleic acid molecule together with Krieg's immunostimulatory oligonucleotide sequence to produce the instant invention with a reasonable expectation of success. Given Krieg's teaching of the routine and conventional nature of using an immunostimulatory oligonucleotide in a pharmaceutical composition for the purpose of immunostimulation, one of skill in the art would have been motivated to produce the instant invention for the expected benefit of further enhancing the immune response to Sanger's product.

Claim 42 is *prima facie* obvious over the prior art of record.

Remarks

16) Claims 32, 37-43, 45, 67, 68 and 70 stand rejected. Claims 30, 31, 33 and 69 are allowable. Claim 44 stands objected to as being dependent from a rejected claim.

17) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO TC 1600 Fax Center which receives papers 24 hours a day, seven days a week. The transmission of such papers by facsimile must conform with the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The RightFax number for submission of before-final amendments is (703) 872-9306. The RightFax number for submission of after-final amendments is (703) 872-9307.

18) Any inquiry concerning this communication or earlier communication(s) from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (703) 308-9347 or (571) 272-0854. A message may be left on the Examiner's voice mail service. The Examiner can normally be reached Monday through Friday from 7.15 a.m to 4.15 p.m. except one day each bi-week which would be disclosed on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909 or (571) 272-0864.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

January, 2004

S. DEVI, PH.D.
PRIMARY EXAMINER

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RESULT    1
ID    VBOR_LAMBD      STANDARD;      PRT;    97 AA.
AC    P26814;
DT    01-AUG-1992 (REL. 23, CREATED)
DT    01-AUG-1992 (REL. 23, LAST SEQUENCE UPDATE)
DT    15-DEC-1998 (REL. 37, LAST ANNOTATION UPDATE)
DE    BOR PROTEIN PRECURSOR.
GN    BOR.
OS    BACTERIOPHAGE LAMBDA.
OC    VIRUSES; DSDNA VIRUSES, NO RNA STAGE; TAILED PHAGES; SIPHOVIRIDAE;
OC    LAMBDA PHAGE GROUP.
RN    [1]
RP    SEQUENCE FROM N.A.
RX    MEDLINE; 83189071.
RA    SANGER F., COULSON A.R., HONG G.F., HILL D.F., PETERSEN G.B.;
RT    "Nucleotide sequence of bacteriophage lambda DNA.";
RL    J. MOL. BIOL. 162:729-773(1982).
RN    [2]
RP    CHARACTERIZATION.
RX    MEDLINE; 90363299.
RA    BARONDES J.J., BECKWITH J.;
RT    "A bacterial virulence determinant encoded by lysogenic coliphage
RT    lambda.";
RL    NATURE 346:871-874(1990).
CC    -!- FUNCTION: NOT KNOWN; IS EXPRESSED DURING LYSOGENY IN ESCHERICHIA
CC        COLI.
CC    -!- SUBCELLULAR LOCATION: ATTACHED TO THE MEMBRANE BY A LIPID ANCHOR
CC        (PROBABLE).
CC    -!- SIMILARITY: TO PLASMID INCFI COLV2-K94 ISS PROTEIN.
CC    ---------------------------------------------------------------------
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CC    ---------------------------------------------------------------------
DR    EMBL; X55792; G288764; -.
KW    LIPOPROTEIN; MEMBRANE; SIGNAL.
FT    SIGNAL         1     16       POTENTIAL.
FT    CHAIN         17     97       BOR PROTEIN.
FT    LIPID         17     17       N-ACYL DIGLYCERIDE (POTENTIAL).
SQ    SEQUENCE   97 AA;  10386 MW;  E49260BD CRC32;

  Query Match              87.6%;  Score 634;  DB 1;  Length 97;
  Best Local Similarity    90.7%;  Pred. No. 4.49e-135;

  Matches   88;  Conservative    7;  Mismatches   2;  Indels   0;  Gaps   0;

Db       1 MKKMLLATALALLITGCAQQTFTVQNKPAAVAPKETITHHFFVSGIGQKKTVDAAKICGG 60
           |||||:::|||:|||||||||||| |||:||:|||||||||||||| ||||||||||
Qy       6 MKKMLFSAALAMLITGCAQQTFTVGNKPTAVTPKETITHHFFVSGIGQEKTVDAAKICGG 65

Db      61 AENVVKTETQQTFVNGLLGFITLGIYTPLEARVYCSQ 97
           |||||||||||||||||||:||||||||||||||||
Qy      66 AENVVKTETQQTFVNGLLGFITFGIYTPLEARVYCSQ 102
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